



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,188	02/20/2001	John F.T. Conroy		3777

7590 03/29/2006  
Pamela M. Norris  
1509 Still Meadow Cove  
Charlottesville, VA 22901

EXAMINER

NAFF, DAVID M

ART UNIT PAPER NUMBER

1651

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.



UNITED STATES PATENT AND TRADEMARK OFFICE

---

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

**MAILED**  
**MAR 29 2006**  
**GROUP 1600**

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 09/785,188  
Filing Date: February 20, 2001  
Appellant(s): CONROY ET AL.

John F Conroy, Mary E. Power and Pamela M. Norris  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed January 23, 2006  
appealing from the Office action mailed August 24, 2004.

Art Unit: 1651

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

Art Unit: 1651

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

4,148,689

Hino et al

4-1979

Uo et al. "Immobilization of Yeast Cells in Porous Silica Carrier with Sol-Gel Process" Journal of the Ceramic Society of Japan, Vol. 100, No. 4 (1992), pp. 426-429,

Klein et al. "Effect of Water on Acid- and Base-Catalyzed Hydrolysis of Tetraethylorthosilicate (TEOS)" Better Ceramics Through Chemistry, Vol. 32 (1984), pp. 33-39.

Rao et al. "Influence of Molar Ratios of Precursor, Catalyst, Solvent and Water on Monolithicity and Physical Properties of TMOS Silica Aerogels" Journal of Sol-Gel Science and Technology, Vol. 3 (1994), pp. 205-217.

Schmidt et al. "Principles of Hydrolysis and Condensation Reaction of Alkoxysilanes" Journal of Non-Crystalline Solids, Vol. 63 (1984), pp. 1-11.

Art Unit: 1651

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 103***

Claims 26, 28, 29 and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uo et al in view of Hino et al (4,148,689).

Claim 26 is drawn to a method comprising mixing a vegetative cell into a sol, mixing a dispersant into the sol to cause macropores in a gel formed by the sol and gelling the sol. Claim 28 requires gel comprising a macroporous solid network formed by condensing hydroxy metallates from a sol solution containing a bacterial cell. Claims 29 and 31-36 are drawn to the same type of gel as claim 28 except that the cell is a vegetative cell.

Uo et al disclose immobilizing yeast cells in a porous silica gel carrier using the sol-gel process by forming a mixture containing tetramethoxysilane (TMOS), water, methanol and polyethylene glycol (PEG), pre-hydrolyzing to form a sol, adding yeast cells in the form of spores, and forming a gel. See abstract (page 426, left col), and paragraph 2.3 on page 427. The porous gel can have pore diameters ranging from 0.1  $\mu\text{m}$  to 10  $\mu\text{m}$  (page 429, right col, under "Conclusion"). This pore

Art Unit: 1651

size range encompasses macropores (page 427, right col, paragraph 3.1, line 4 of the paragraph). Yeast spores are used since the spores are durable to organic solvents (page 427, left col, paragraph 2.2).

Hino et al disclose producing a silica gel containing immobilized microbial cells (col 1, lines 7-15 and col 4, lines 30-47) by hydrolyzing an alkoxysilane in combination with a water-soluble polymer to form a sol, adding microbial cells which can be bacteria or yeast cells (col 7, lines 1-47) and gelling the sol to obtain a gel with the microbial cells immobilized therein.

The method of claim 26 and gel of claim 29 are the same as the method and resultant gel disclosed by Uo et al except that the claims require a vegetative cell instead of yeast spores. The gel of claim 28 is the same as obtained by Uo et al except that the claim requires a bacterial cell instead of a yeast cell.

It would have been obvious to use vegetative yeast cells in place of the yeast spores in the method of Uo et al as suggested by Hino et al carrying out a similar sol-gel process to produce a silica gel containing immobilized microbial cells which can be yeast cells or bacteria cells without requiring the cells to be in spore form. Using vegetative cells not in spore form would

Art Unit: 1651

have been expected to be advantageous due to simplification resulting from not having to convert vegetative cells to spores and then convert the spores to vegetative cells to provide the cells in active form for use. This simplification would have been motivation to use vegetative cells instead of spores.

While using vegetative cells may result in the cells immobilized in the silica gel having less activity due to the cells being less durable to the organic solvent, the present claims require nothing that would avoid the this adverse affect. The claims do not require the cells immobilized to have a certain amount of activity, and the claims do not exclude the immobilizing method resulting in immobilized cells having less activity than before the cells are immobilized. The claims recite "comprising", and do not exclude the organic solvent (methanol) used by Uo et al, and the specification discloses (paragraph bridging pages 4 and 5) that a sol containing an organic solvent can be formed followed by mixing a biological material and dispersant with the sol, and forming a macroporous gel. When the advantage of vegetative cells resulting in simplification of the process of Uo et al is considered more desirable than the advantage of spores being more durable in the process, the use of vegetative cells would have been clearly obvious. Substituting one advantage for another is well within the ordinary skill of the

Art Unit: 1651

art, even through obtaining each advantage may incur a disadvantage. The gel of Uo et al will inherently transmit light as required by claims 31-35.

Substituting a bacterial cell for the yeast cell of Uo et al as in claim 28 would have been obvious in view of Hino et al immobilizing bacterial cells or yeast cells in a silica gel carrier. The type of cell immobilized will depend on cell function desired, and when the function of a bacterial cell is desired, it would have been obvious to immobilize a bacterial cell. Claim 28 does not require the bacterial cell to be vegetative, and the bacterial cell can be in spore form like the yeast cells of Uo et al.

***Claim Rejections - 35 USC § 103***

Claims 15-23, 25 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 26, 28, 29 and 31-36 above, and further in view of Klein et al and Rao et al.

The claims require a sol containing P moles of hydroxy metallate, W moles of water, dispersant to cause macropores in a gel formed from the sol and a biological material, and a ratio of W:P greater than 25:1.



Art Unit: 1651

Klein et al disclose the effect of water on hydrolysis of TEOS and Rao et al disclose the influence ratios of precursor, catalyst, solvent and water on properties of silica aerogels.

It would have been a matter of obvious choice and require only limited routine experimentation to select a preferred optimum amount of water in Uo et al in view of the disclosures of Klein et al and Rao et al as to the effect of varying the water content.

***Claim Rejections - 35 USC § 103***

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 15-23, 25 and 37-39 above, and further in view of Schmidt et al.

The claim requires an organic solvent to be produced as a by-product of hydrolysis.

Schmidt et al disclose that hydrolysis of alkoxysilanes produces an alcohol. See reaction formula (1) (page 1).

It would have been obvious that hydrolysis in Uo et al will produce an alcohol as taught by Schmidt et al.

**(10) Response to Argument**

***Response to Arguments (claims 26 and 29)***

Beginning on page 4 of the brief, appellants urge that claims 26 and 29 are not obvious since Uo et al suggest that the gelation solution used will be toxic to vegetative cells due to

Art Unit: 1651

the antimicrobial activity of methanol present because Uo et al use yeast spores due to their durability to organic solvents.

This argument is unpersuasive since the present claims fail to exclude the organic solvent of Uo et al, and the specification discloses (paragraph bridging pages 4 and 5) that an organic solvent can be present. Furthermore, the claims do not require the vegetative cells immobilized to retain a certain amount of their activity before immobilizing, and the claims encompass the activity of vegetative cells being reduced due to the presence of an organic solvent. The disclosure by Uo et al that yeast spores are more durable to organic solvents does not suggest that vegetative cells will be totally inactivated by the solvent, but rather that vegetative cells are less durable and may not have as high an activity after immobilization as when using spores. As noted above, the claims do not require the vegetative cells after immobilization in the gel to retain a certain amount of the cell activity before immobilization. The claims encompass the vegetative cells losing a substantial amount of activity during immobilization, or even having no activity after immobilization.

Even if the claims excluded the methanol of Uo et al, Hino et al suggest that the methanol can be omitted by performing the same type of process as Uo et al and not requiring methanol or

Art Unit: 1651

other organic solvent in the sol gelled. As in Uo et al, the sol of Hino et al can contain polyethylene glycol (col 4, line 62), and Hino et al disclose the polyethylene glycol as a water-soluble polymer. Thus, it is clear from Hino et al that the methanol of Uo et al can be omitted and still obtain a silica gel immobilizing cells.

Appellants (page 5) refer to a publication by Block (indicated as previously submitted in a response of July 25, 2003) as showing the toxicity of alcohols such as methanol to vegetative cells. Appellants point out that the gelation solution of Uo et al contains 45-55 vol.% methanol, and the cells are exposed to this solution for one day, and Block describes that 65 vol.% methanol is microbicidal to both *Staphylococcus aureus* and *Eschedrichia coli* in under 1 minute, and even 9 vol.% methanol is effective at inhibiting *S. aureus*.

This argument is unpersuasive since Uo et al do not expose the cells to the gelation solution for one day. As is apparent from the paragraph bridging the columns on page 427 of Uo et al, pre-hydrolysis is carried out for one day, and then the yeast spores are added, and the solution gels. The cells are exposed to the solution only until the solution gels, after which the cells are not exposed to the solution. According to Hino et al (col 8, lines 25-28) in a similar process, gelling takes 10-30

Art Unit: 1651

minutes or 10-20 minutes. Furthermore, the gelation solution of Uo et al does not contain only methanol and water as the solution in Block, but also contains TMOS and PEG which could lessen the microbicidal affect methanol. Additionally, Uo et al use 45-55 vol.% methanol, and this amount is substantially less than the 65 vol.% disclosed by Block as being microbicidal. In fact, 45 vol.% is 20 vol.% less than 65 vol.%. Exposing vegetative cells to the gelation solution of Uo et al for 10 minutes until the solution gels when the solution contains 45 vol.% would appear leave a substantial number of cells active, even through some killing of cells may occur. As noted above, the claims do not require a certain number of cells to be alive and active in the gel after immobilizing, and the claims do not exclude the presence of methanol. Moreover, if the methanol used by Uo et al was found to kill too many vegetative cells to produce immobilized cells that are useable, it would have been obvious to omit the methanol as suggested by Hino et al performing a process similar to that of Uo et al for immobilizing cells, and not requiring an organic solvent.

Appellants urge (page 6) that Hino et al describe vegetative cells being susceptible to the antimicrobial activity of alcohols by describing extrusion casting in isopropyl alcohol and obtaining 61% activity as compared to 84-90% activity when

Art Unit: 1651

not casting. However, Hino et al found the 61% activity to be acceptable and useable even through the activity is lower. The present claims do not exclude obtaining a lowered activity as disclosed by Hino et al. Furthermore, Hino et al obtaining a substantial amount of cell activity after contacting with an alcohol supports that a substantial amount of vegetative cell activity will result after contacting vegetative cells with methanol in the process of Uo et al.

In the paragraph bridging pages 7 and 8, appellants urge that not excluding the organic solvent is irrelevant. However, it is not irrelevant since if not excluded, the claims encompass using methanol as in Uo et al

Appellants urge (page 8) that there is nothing in the prior art to lead one of ordinary skill in the art to ignore the toxicity of the gelation solution of Uo et al to vegetative cells. However, Hino et al apparently ignored this toxicity since an alcohol was used in casting, even through it lowered vegetative cell activity to 61.1% (Table 7, col 16). Additionally, in Table 7, acetone lowered the activity to 54%, and this activity was considered to be acceptable since it was above 50% (col 16, line 4).

Appellants urge (paragraph bridging pages 9 and 10) that Hino et al does not form macropores and does not suggest that

Art Unit: 1651

methanol can be omitted in Uo et al and still obtain macropores. However, it is the PEG and not methanol in Uo et al that forms the macropores. Hino et al disclose that PEG is a water-soluble polymer (col 4, line 62), and it would have been obvious from Hino et al that PEG will be soluble in the process of Uo et al without methanol. There is inadequate evidence to establish that the methanol of Uo et al is critical to obtaining macropores. Even if present, the claims do not exclude its toxicity, and Hino et al disclose obtaining acceptable activity of over 50% even when a toxic solvent is used. The rejection is not based on Uo et al alone but on Uo et al in combination with Hino et al.

Appellants (page 11, fourth paragraph) refer to Figure 1 of the specification as disclosing distilling off alcohol by-products to reduce toxicity to cells being immobilized. However, the claims do not require removing alcohol by distilling to reduce toxicity to cells immobilized.

***Response to Arguments (claim 28)***

Beginning on page 12, appellants present arguments as to claim 28 being unobvious. Claim 28 encompasses the bacterial cell being either vegetative cells or spores. In regard to the use of vegetative cells and a toxic solvent, the type of comments set forth above apply.

Art Unit: 1651

Appellants urge that neither Uo et al nor Hino et al describe bacterial spores. However, it is well known in the art that bacteria can form spores. The only reason that Uo et al use yeast cells is because of they have use in fermentation technology (page 426, under "Introduction"). When the function of a bacteria cell is desired, it would have been obvious to substitute bacteria cells for the yeast cells in Uo et al since in a similar process of immobilizing cells in silica gel disclosed by Hino et al, bacteria cells or yeast cells can be immobilized in the silica gel. The use of vegetative bacteria cells would have been obvious for reasons set forth above in regard to the use of vegetative yeast cells in Uo et al. The use of bacteria spores would have been obvious to obtain the greater durability of the spores to an organic solvent as suggested by Uo et al. There is seen nothing to lead one to believe that bacteria spores will not have the greater durability to organic solvents as disclosed by Uo et al for yeast cells.

Appellants urge that the gels of Uo et al and Hino et al are not similar since Hino et al does not produce a macroporous gel. However, the gel of Hino et al is porous, since if not porous, a substrate would not be able to reach cells in the gel to be acted on by the cells in a process of use. Additionally,

Art Unit: 1651

if the gel is not porous, nutrients could not reach the cells in the gel. The gel having larger pores that are macropores is not be substantial difference. Note that the pores of the gel of Uo et al can vary from 0.1  $\mu\text{m}$  to 10  $\mu\text{m}$ . As in Uo et al, the process of Hino et al (col 4, lines 30-41) can involve forming a solution of a tetralkoxysilane and PEG, hydrolyzing the tetraalkoxysilane to produce a sol, adding cells to the sol, and gelling the sol to entrap the cells in the gel formed. The PEG of Uo et al, like that of Hino et al, is water soluble since Uo et al (page 427, left col, lines 6-8) use water to leach out the PEG after gelling. Hino et al not having methanol present in the solution containing tetralkoxysilane and PEG, supports that the methanol of Uo et al can be omitted if desired. Uo et al disclose pore size depending on PEG content and water content in the gelling solution (page 427, paragraphs 3.1 and 3.2), and there is no disclosed dependency of pore size on methanol content. Pore size increases with decreasing PEG content and increasing water content (Page 428, Figures 1-4 of Uo et al).

***Response to Arguments (claim 15)***

The type of comments set forth above in response to arguments in regard to the use of vegetative cells, bacterial cells, spores and/or toxic solvent, also apply to this rejection where necessary.



Art Unit: 1651

Appellants urge that Klein et al use approximately 65% ethanol when the ratio of water to hydroxy metallate is 32:1. However, claim 15 does not exclude organic solvents and microbial spores such as yeast spores. It is clear from Uo et al that methanol can be used in combination with yeast spores, and other microbial spores would have been expected to also be resistant to methanol. Moreover, to avoid the toxicity of an organic solvent, it would have been obvious to reduce the amount of solvent used so as not to kill an undue number of cells when vegetative cells are present, and being willing to incur an adverse affect from reducing the amount of solvent. Also, as noted above, the claims encompass the biological material after immobilization having no activity, or having very low activity. Klein et al disclose that high water solutions are more completely hydrolyzed and condensed (last complete sentence on page 38), that increased water levels will increase the rate of hydrolysis (page 39, under "Conclusions"), and that a high water acid-catalyzed solution should produce a gel which has a high surface area (page 39, lines 7-9). To obtain these results, it would have been obvious to use a higher amount of water than used by Uo et al. Additionally, Uo et al disclose that increasing water content increases pore size, and it would have

Art Unit: 1651

been obvious to increase water content when a larger pore size is desired.

**Response to Arguments (claim 24)**

No arguments have been presented traversing the rejection of claim 24 over Schmidt et al.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,




David M. Naff  
Primary Examiner  
Art Unit 1651

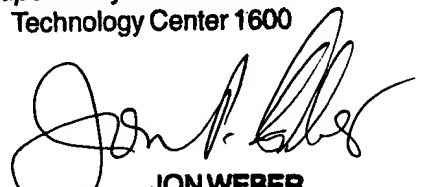
Conferees:

Michael G. Wityshyn

Jon P. Weber



Michael G. Wityshyn  
Supervisory Patent Examiner  
Technology Center 1600



JON WEBER  
SUPERVISORY PATENT EXAMINER